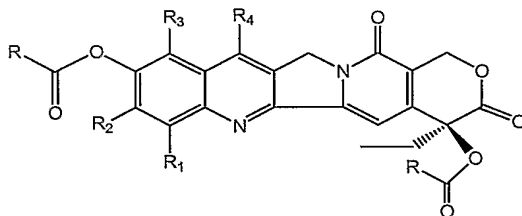


WHAT IS CLAIMED IS:

1. A di-ester derivative of camptothecin having the following general structure:



wherein

R_1 , R_2 , R_3 , and R_4 , which can be the same or different, are hydrogen, halogen, C_1 - C_{20} alkyl, C_1 - C_8 alkoxy, C_4 - C_{20} aryl, and C_1 - C_{20} silyl,

each R can be the same or different and is C_1 - C_{30} alkyl, C_2 - C_{22} alkenyl, C_4 - C_{30} aryl, $(CH_2)_nOR_5$, $(CH_2)_nSR_5$, $(CH_2)_nNR_5R_6$, $(CH_2)_nCOR_7$,

wherein,

R_5 and R_6 , which can be the same or different, are C_1 - C_8 alkyl, C_1 - C_6 alkenyl, and C_4 - C_{10} aryl,

R_7 is hydroxy, C_1 - C_{20} alkyl, C_1 - C_6 alkenyl, C_1 - C_6 alkoxy, C_4 - C_{20} aryl, or NR_8R_9 ,

wherein,

R_8 and R_9 , which can be the same or different are C_1 - C_6 alkyl,

and n is an integer of 1 to 8,

and pharmaceutically acceptable salts hereof.

2. A compound of claim 1 wherein each R can be the same or different and is C_1 - C_{20} alkyl, C_2 - C_6 alkenyl, or C_4 - C_{20} aryl.

3. A pharmaceutical composition, comprising an effective amount of the camptothecin di-ester derivatives of claim 1 and a pharmaceutically acceptable carrier or diluent.

4. A pharmaceutical composition, comprising an effective amount of the camptothecin di-ester derivatives of claim 2 and a pharmaceutically acceptable carrier or diluent.

5. The di-ester of claim 1, wherein each of R_1 , R_2 , R_3 , and R_4 is H, and R is C_3 - C_{30} alkyl.
6. The di-ester of claim 2, wherein each of R_1 , R_2 , R_3 , and R_4 is H, and R is C_1 - C_{20} alkyl.
7. The di-ester of claim 1, wherein each of R_1 , R_2 , R_3 , and R_4 is H, and R is C_2 - C_{22} alkenyl.
8. The di-ester of claim 2, wherein each of R_1 , R_2 , R_3 , and R_4 is H, and R is C_2 - C_6 alkenyl.
9. The di-ester of claim 1, wherein each of R_1 , R_2 , R_3 and R_4 is H, and R is $(CH_2)_nOR_5$,
wherein,
 R_5 is C_1 - C_6 alkyl, C_2 - C_6 alkenyl, or C_4 - C_{10} aryl, and
 n is an integer of 1 to 2.
10. The di-ester of claim 1, wherein each of R_1 , R_2 , R_3 and R_4 is H, and R is $(CH_2)_nSR_5$,
wherein,
 R_5 is C_1 - C_6 alkyl, C_2 - C_6 alkenyl, or C_4 - C_{10} aryl, and
 n is an integer of 1 to 2.
11. The di-ester of claim 1, wherein each of R_1 , R_2 , R_3 and R_4 is H, and R is $(CH_2)_nNR_5R_6$,
wherein,
 R_5 and R_6 are independently hydrogen, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, or C_4 - C_{10} aryl,
and
 n is an integer of 1 to 2.
12. The di-ester of claim 1, wherein each of R_1 , R_2 , R_3 and R_4 is H, and R is $(CH_2)_nCOR_7$,
wherein,
 R_7 is hydroxy, C_1 - C_6 alkyl, C_2 - C_6 alkenyl, or C_4 - C_{10} aryl, and

n is an integer of 2 to 4.

13. The di-ester of claim 1, wherein each of R_1 , R_2 and R_3 is H, R_4 is CH_2CH_3 , and R is $\text{C}_1\text{--C}_{30}$ alkyl.

14. The di-ester of claim 2, wherein each of R_1 , R_2 and R_3 is H, R_4 is CH_2CH_3 , and R is $\text{C}_1\text{--C}_{20}$ alkyl.

15. The di-ester of claim 1, wherein each of R_1 , R_2 and R_3 is H, R_4 is CH_2CH_3 , and R is $\text{C}_2\text{--C}_{22}$ alkenyl.

16. The di-ester of claim 2, wherein each of R_1 , R_2 and R_3 is H, R_4 is CH_2CH_3 , and R is $\text{C}_2\text{--C}_6$ alkenyl.

17. The di-ester of claim 1, wherein each of R_1 , R_2 and R_3 is H, R_4 is CH_2CH_3 , and R is $\text{C}_4\text{--C}_{30}$ aryl.

18. The di-ester of claim 2, wherein each of R_1 , R_2 and R_3 is H, R_4 is CH_2CH_3 , and R is $\text{C}_4\text{--C}_{20}$ aryl.

19. The di-ester of claim 1, wherein each of R_1 , R_2 and R_3 is H, R_4 is CH_2CH_3 , and R is $(\text{CH}_2)_n\text{OR}_5$,

wherein,

R_5 is $\text{C}_1\text{--C}_6$ alkyl, $\text{C}_2\text{--C}_6$ alkenyl, or $\text{C}_4\text{--C}_{10}$ aryl, and

n is an integer of 1 to 2.

20. The di-ester of claim 1, wherein each of R_1 , R_2 and R_3 is H, R_4 is CH_2CH_3 , and R is $(\text{CH}_2)_n\text{SR}_5$,

wherein,

R_5 is $\text{C}_1\text{--C}_6$ alkyl, $\text{C}_2\text{--C}_6$ alkenyl, or $\text{C}_4\text{--C}_{10}$ aryl, and

n is an integer of 1 to 2.

21. The di-ester of claim 1, wherein each of R_1 , R_2 and R_3 is H, R_4 is CH_2CH_3 , and R is $(\text{CH}_2)_n\text{NR}_5\text{R}_6$,

wherein,

R_5 and R_6 are independently hydrogen, C_1-C_6 alkyl, C_2-C_6 alkenyl, or C_4-C_{10} aryl, and

n is an integer of 1 to 2.

22. The di-ester of claim 1, wherein each of R_1 , R_2 and R_3 is H, R_4 is CH_2CH_3 , and R is $(CH_2)_nCOR_7$,

wherein,

R_7 is hydroxy, C_1-C_6 alkyl, C_2-C_6 alkenyl, or C_4-C_{10} aryl, and

n is an integer of 2 to 4.

23. The di-ester of claim 1, wherein each of R_1 , R_2 and R_3 is H, R_4 is $Si(CH_3)_2C(CH_3)_3$, and R is C_1-C_{30} alkyl.

24. The di-ester of claim 2, wherein each of R_1 , R_2 and R_3 is H, R_4 is $Si(CH_3)_2C(CH_3)_3$, and R is C_1-C_{20} alkyl.

25. The di-ester of claim 1, wherein each of R_1 , R_2 and R_3 is H, R_4 is $Si(CH_3)_2C(CH_3)_3$, and R is C_2-C_{22} alkenyl.

26. The di-ester of claim 2, wherein each of R_1 , R_2 and R_3 is H, R_4 is $Si(CH_3)_2C(CH_3)_3$, and R is C_2-C_6 alkenyl.

27. The di-ester of claim 1, wherein each of R_1 , R_2 and R_3 is H, R_4 is $Si(CH_3)_2C(CH_3)_3$, and R is C_4-C_{30} aryl.

28. The di-ester of claim 2, wherein each of R_1 , R_2 and R_3 is H, R_4 is $Si(CH_3)_2C(CH_3)_3$, and R is C_4-C_{20} aryl.

29. The di-ester of claim 1, wherein each of R_1 , R_2 and R_3 is H, R_4 is $Si(CH_3)_2C(CH_3)_3$, and R is $(CH_2)_nOR_5$;

wherein,

R_5 is C_1-C_6 alkyl, C_1-C_6 alkenyl, or C_4-C_{10} aryl, and

n is an integer of 1 to 2.

30. The di-ester of claim 1, wherein each of R_1 , R_2 and R_3 is H, R_4 is $Si(CH_3)_2C(CH_3)_3$, and R is $(CH_2)_nSR_5$,

wherein,

R_5 is C_1-C_6 alkyl, C_1-C_6 alkenyl, or C_4-C_{10} aryl, and
 n is an integer of 1 to 2.

31. The di-ester of claim 1, wherein each of R_1 , R_2 and R_3 is H, R_4 is $Si(CH_3)_2C(CH_3)_3$, and R is $(CH_2)_nNR_5R_6$,

wherein,

R_5 and R_6 are independently hydrogen, C_1-C_6 alkyl, C_1-C_6 alkenyl, or C_4-C_{10} aryl,
and
 n is an integer of 1 to 2.

32. The di-ester of claim 1, wherein each of R_1 , R_2 and R_3 is H, R_4 is $Si(CH_3)_2C(CH_3)_3$, and R is $CH_2)_nCOR_7$,

wherein,

R_7 is hydroxy, C_1-C_6 alkyl, C_2-C_6 alkenyl, or C_4-C_{10} aryl, and
 n is an integer of 2 to 4.

33. The di-ester of claim 1, wherein R_1 is $CH_2N(CH_3)_2$, each of R_2 , R_3 and R_4 is H, and R is C_1-C_{30} alkyl.

34. The di-ester of claim 2, wherein R_1 is $CH_2N(CH_3)_2$, each of R_2 , R_3 and R_4 is H, and R is C_1-C_{20} alkyl.

35. The di-ester of claim 1, wherein R_1 is $CH_2N(CH_3)_2$, each of R_2 , R_3 and R_4 is H, and R is C_2-C_{22} alkenyl.

36. The di-ester of claim 2, wherein R_1 is $CH_2N(CH_3)_2$, each of R_2 , R_3 and R_4 is H, and R is C_2-C_6 alkenyl.

37. The di-ester of claim 1, wherein R_1 is $CH_2N(CH_3)_2$, each of R_2 , R_3 and R_4 is H, and R is C_4-C_{30} aryl.

38. The di-ester of claim 2, wherein R_1 is $CH_2N(CH_3)_2$, each of R_2 , R_3 and R_4 is H, and R is C_4-C_{20} aryl.

39. The di-ester of claim 1, wherein R_1 is $\text{CH}_2\text{N}(\text{CH}_3)_2$, each of R_2 , R_3 and R_4 is H, and R is $(\text{CH}_2)_n\text{OR}_5$,

wherein,

R_5 is $\text{C}_1\text{--C}_6$ alkyl, $\text{C}_2\text{--C}_6$ alkenyl, or $\text{C}_4\text{--C}_{10}$ aryl, and
n is an integer of 1 to 2.

40. The di-ester of claim 1, wherein R_1 is $\text{CH}_2\text{N}(\text{CH}_3)_2$, each of R_2 , R_3 and R_4 is H, and R is $(\text{CH}_2)_n\text{SR}_5$,

wherein,

R_5 is $\text{C}_1\text{--C}_6$ alkyl, $\text{C}_2\text{--C}_6$ alkenyl, or $\text{C}_4\text{--C}_{10}$ aryl, and
n is an integer of 1 to 2.

41. The di-ester of claim 1, wherein R_1 is $\text{CH}_2\text{N}(\text{CH}_3)_2$, each of R_2 , R_3 and R_4 is H, and R is $(\text{CH}_2)_n\text{NR}_5\text{R}_6$,

wherein,

R_5 and R_6 are independently hydrogen, $\text{C}_1\text{--C}_6$ alkyl, $\text{C}_1\text{--C}_6$ alkenyl, or $\text{C}_4\text{--C}_{10}$ aryl,
and
n is an integer of 1 to 2.

42. The di-ester of claim 1, wherein R_1 is $\text{CH}_2\text{N}(\text{CH}_3)_2$, each of R_2 , R_3 and R_4 is H, and R is $(\text{CH}_2)_n\text{COR}_7$,

wherein,

R_7 is hydroxy, $\text{C}_1\text{--C}_6$ alkyl, $\text{C}_2\text{--C}_6$ alkenyl, or $\text{C}_4\text{--C}_{10}$ aryl, and
n is an integer of 2 to 4.

43. A method to inhibit the enzyme topoisomerase I comprising administering a composition comprising at least one di-ester of claim 1.

44. A method to inhibit the enzyme topoisomerase I comprising administering a composition comprising at least one di-ester of claim 2.

45. A method to treat cancer in a patient comprising administering a composition comprising at least one di-ester of claim 1 to said patient in an effective amount to treat said cancer.

46. A method to treat cancer in a patient comprising administering a composition comprising at least one di-ester of claim 2 to said patient in an effective amount to treat said cancer.

47. The method of claim 45, wherein said cancer is lung, breast, colon, prostate, melanoma, pancreas, stomach, liver, brain, kidney, uterus, cervix, ovaries, urinary tract, gastrointestinal, or leukemia.

48. The method of claim 46, wherein said cancer is lung, breast, colon, prostate, melanoma, pancreas, stomach, liver, brain, kidney, uterus, cervix, ovaries, urinary tract, gastrointestinal, or leukemia.

49. The method of claim 45, wherein said cancer is solid tumor or blood born tumor.

50. The method of claim 46, wherein said cancer is solid tumor or blood born tumor.

51. The method of claim 45, wherein said composition is administered orally, parenterally, intramuscularly, transdermally or by an airborne delivery system.

52. The method of claim 46, wherein said composition is administered orally, parenterally, intramuscularly, transdermally or by an airborne delivery system.

53. The method of claim 45, wherein said composition is a nanoparticle containing said at least one di-ester of camptothecin.

54. The method of claim 46, wherein said composition is a nanoparticle containing said at least one di-ester of camptothecin.